TERTIARY STRUCTURE OF PEANUT ALLERGEN ARA H 1

ABSTRACT OF THE DISCLOSURE

Allergy to peanut is a significant health problem because of the prevalence and potential severity of the reaction. Ara h 1, a major peanut allergen, has been isolated and characterized and was shown to consist of 626 amino acids and contain 23 linear IgE-binding epitopes, 6-10 residues in length. The amino acids important for peanut-specific IgE binding were determined by synthesizing wild type and mutant peptides with single alanine, glycine or methionine substitutions at each position followed by incubation in pooled serum from patients with peanut hypersensitivity. From this analysis it was determined that amino acids which reside in the midele of the epitope were generally more critical for IgE binding. Furthermore, though polar charged residues occur most frequently within the epitopes. apolar residues were found to be more important for IgE binding. In addition, it was found that each epitope could be mutated resulting in loss of ability to bind IgE with only a single amino acid substitution. To further characterize the epitopes a homology-based molecular model of the Ara h 1 protein was made. The model represents residues 171-586 allowing visualization of epitopes 10-22. The majority of these epitopes appear to be clustered to certain areas of the molecule. Many of the critical amino acids involved in binding are evenly distributed on the surface and not buried in the hydrophobic core. The information from the mutational analysis along with the molecular model will aid in the design of immunotherapies.